REMARKS

Election of Invention

The Examiner has issued a restriction requirement stating that the application claims four distinct inventions. Specifically, the Examiner identifies the four inventions as being:

I. Claims 1-7, drawn to a composition for the diagnosis of a defect of the Wnt/frz/Lrp5, 6 cascade.

II. Claims 8, 9, drawn to a method for identifying a binding partner for Kremen.

III. Claims 10, 11, 12, drawn to a pharmaceutical composition for inhibiting the Wnt cascade.

IV. Claims 13, 14, 15, drawn to a pharmaceutical composition comprising a compound capable of modulating the expression of a nucleic acid.

Pursuant to 37 C.F.R. §1.499, Applicants elect Group II, Claims 8 and 9 and add new claims 16-25 which are dependent from claims 8 or 9. As Inventions I, II, III and IV are related as product and process of use, Applicants reserve the right to rejoinder of the non-elected inventions in the event that the claims directed to the product identified by using the method of claim 8 or 9 are found allowable. Accordingly, claims 1-7 and 10-15 are withdrawn without prejudice.

Applicants also reserve the right pursuant to 35 U.S.C. §121 to file one or more divisional applications directed to the non-elected inventions during the pendency of the present application.

Further Restriction Requirement

The Examiner has also issued a further restriction on groups I-IV which requires Applicants to

I. Further elect Kremen 1 or Kremen 2 or the combination;

II. Further elect a Kremen 1 polypeptide or Kremen 2 polypeptide or the combination;

III. Further elect nucleotide molecule encoding a Kremen 1 or Kremen 2 polypeptide or the combination, an activator/agonist of a Kremen 1 polypeptide or a Kremen 2 polypeptide or the combination, a binding partner of Kremen 1 polypeptide, or Kremen 2 polypeptide, or the combination; and

IV. Further elect a nucleic acid molecule encoding human Kremen 1 or human Kremen 2.

The Examiner stated that this is not an election of species; and the nucleic acid molecules in groups I, III and IV encode different protein sequences and are structurally distinct chemical compounds and are unrelated to one another. Applicants respectfully traverse the Examiner's grounds for such a further restriction requirement based on the following reasons.

First, Kremen 1 and Kremen 2 are not independent and distinct in the context of the elected method for identifying a compound for modulating the Wnt signal cascade based on identifying a binding partner to Kremen 1 and/or Kremen 2. In the claimed method, Kremen 1 and Kremen 2 are related with each other and are not distinct, because both bind with high affinity to the polypeptides Dkk1 and Dkk2 (*see* Example 2, Fig. 3). Both Kremen 1 and Kremen 2 can be regarded as a receptor for the Dkk polypeptides and the biological function of Kremen is the mediation of inhibition of the Wnt-LRP signal cascade via Dkk polypeptides. Hence, Kremen 1 and Kremen 2 have the same biological function in modulating the Wnt signal cascade.

Secondly, Kremen 1 and Kremen 2 are highly homologous proteins (as can be seen from Figure 2 of the application) and thus an examination of both together would not represent an

additional burden on the Examiner. Regarding the elected invention of a screening assay you would expect a binding partner for Kremen 1 to equally recognize Kremen 2 due to their high level of homology.

Finally, Applicants respectfully remind the Examiner that this application is an U.S. national stage application of an International PCT-Application. Therefore, PCT Rule 13.2 should be applied also for the assessment of the unity of the invention of the elected group of inventions. The cited reference Nakamura et al. (Biochim Biophys Acta. (2001) 1518(1-2):63-72) does not teach or suggest a method for identifying a compound for modulating the Wnt signal cascade based on identifying a binding partner to Kremen 1 and/or Kremen 2. Therefore, the cited reference cannot anticipate the single general inventive concept of the elected group of invention.

In summary, in view of the elected group II of inventions drawn to a method for identifying a compound for modulating the Wnt signal cascade based on identifying a binding partner to Kremen 1 and/or Kremen 2, Kremen 1 and Kremen 2 should be regarded as being of similar nature, and thus a further restriction to one of Kremen 1 or Kremen 2 is not necessary. Withdrawal of the further restriction requirement to Kremen 1 or Kremen 2 is therefore respectfully requested.

CONCLUSION

Applicants submit that this paper fully addresses the Restriction Requirement mailed July 10, 2007. Should the Examiner have any questions, the Examiner is encouraged to contact the undersigned attorney at (650) 565-3856. The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 23-2415 (Docket No. 31304-702.831).

Respectfully submitted,

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